REMARKS/ARGUMENTS

Claims 11, 22-25, and 40-43 are pending.

Claims 1-10, 12-21, and 26-39 have been cancelled.

Claims 40-43 have been added.

Support for the amendment to claim 11 is found in claims 1 and 7, and page 14 of the specification as originally filed. Support for claim 40 is found at page 43; support for claims 41-43 is found in claims 9-10 and pages 53-56 of the specification, as originally filed. Claim 22 is rewritten in an independent form. No new matter is believed to be added by the submission of amended claims.

The rejections based on Arkinstall have been maintained. It is requested that the rejections be withdrawn as Arkinstall, by itself or combined with the other cited publications neither describes or suggests, explicitly or inherently, the treatment of type II diabetes with the sulfonamide compounds of formula (I) of claim 11.

Also, Arkinstall, by itself or combined with the other cited publications neither describes or suggests, explicitly or inherently, the treatment of type II diabetes with 4-chloro-N-[(5-{[4-(butylamino)piperidin-1-yl]sulfonyl}thien-2-yl)methyl]benzamide of claim 40 and specific compounds of claim 22 as presented here.

Further, Arkinstall does not teach selecting specific sulfonamide derivatives of claim 11, 22, and 4-chloro-N-[(5-{[4-(butylamino)piperidin-1-yl]sulfonyl}thien-2-yl)methyl]benzamide of claim 40. Arkinstall describes generic compounds broadly encompassing the claimed sulfonamide compounds, but specifically describes different compounds.

The legal requirement for inherency is that "each and every time" the drug is administered in the prior art (in autoimmune patients) the administration must also treat what

we claim here (diabetes type II). Autoimmune diseases relate to a vast spectrum of disorders involving the thyroid, lupus, multiple sclerosis, rheumatoid arthritis and others (see the attached listing as an example). Type-II diabetes is not known to be an autoimmune disease. Thus, when an administering compound as taught by Arkinstall, one would not necessarily, each and every time, also treat Type-II diabetes as claimed.

As has been previously discussed, Arkinstall discloses that the JNK signaling pathway is implicated in cell proliferation and could play an important role in autoimmune diseases [0010]. Arkinstall shows that the disclosed generic compounds modulate the JNK pathway as JNK inhibitors, notably JNK2 and JNK3, and are useful for the treatment of the immune and neuronal system disorders [0107], [0135]-[0140].

Although Bennett discloses that one JNK inhibitor (CC105 small molecule) has potential in treating insulin resistance and obesity, it does not mean that all Arkinstall compounds of general formula I are necessarily effective for treating type II diabetes.

Bozyczko-Coyne, Curr. Drug Target – CNS & Neurol. Disorders, 1:31-49, 42-43 (2002), shows that the JNK pathway is very complex, involves many levels of regulations, genes, proteins, and disorders. The JNK pathway is implicated in a large number of physiological and pathological functions. See Bozyczko-Coyne, at 43-43. Moreover, the complexity of the organization and regulation at all levels within the JNK signaling cascade continues to evolve. Further, because of the complex cross talk within this signaling cascade as well as its cell type and response specific modulation, it is difficult to predict potential adverse events that might arise from pathway inhibition (Bozyczko-Coyne, page 43). Owing to the breadth of physiological functions mediated via signaling through the JNK family, direct inhibition at the level of the JNK could prove to have liabilities (Bozyczko-Coyne, page 31. right col.).

Therefore, Bennett at best suggests to try the JNK inhibitors for treatment type II diabetes (one of many disorders modulated via the JNK pathway), but does not support the conclusion that all Arkinstall compounds do treat a type II diabetes.

The Arkinstall compounds display inhibitory activity of the JNK pathway. However, Arkinstall only describes using the compounds for treating disorders of the autoimmune and neuronal system, see [0001], [0017], and [0135]-[0140]. Arkinstall does not enable treating all disorder related to the inhibition of the JNK pathway. Arkinstall does not provide sufficient nexus between autoimmune and neuronal disorders, and type II diabetes so that they are substantially related and can be treated with the same compounds.

In contrast, this specification describes using the claimed specific compounds in *in vivo* assay in db/db mice to determine anti-diabetic effect of the test compounds in a model of postprandial glycemia (page 60-61). The experiment on pages 60-61 shows that the blood glucose level and blood insulin were decreased in the treated animals compared to the untreated animals.

The obviousness rejection combining Sterne and Weber with Arkinstall is largely to allege that the supplemental drugs were known and therefore obvious to use with Arkinstall. Although Applicants respectfully disagree with the supposition of the rejection for the sake of brevity it is again stressed that as Arkinstall neither explicitly or inherently describe the treatment of type II diabetes as claimed, the obviousness rejection based on the combination of citations is inapplicable to the claims.

Applicants request that the rejections based on Arkinstall be withdrawn.

A similar argument as discussed applies to the obviousness type-double patenting rejections that have been maintained.

Claims 11-25 are rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-36 of co-pending application 10/070,954; claims 1-27 of application 10/088,074; claim 1 of application 10/088,090; claims 1-8 and 14 of application 10/381,197; claims 1-8 and 14 of application 10/381,200; claims 1-10, 12, and 16 of application 10/381,665; and claim 1-11 and 17 of application 10/484,744.

The claims of application 10/088,074 are directed to a generic sulfonyl hydrazide compound comprising the species claimed in this application. The compounds of the appl. '074 are useful for treating diseases of the autoimmune and neuronal system. The appl. '074 does not disclose that the sulfonyl hydrazide compounds are effective for treating type II diabetes. The appl. '074 does not provide sufficient nexus between autoimmune and neuronal disorders and type II diabetes so that they are substantially related and can be treated with the same compounds. Further, the appl. '074 does not suggest selecting the specific compounds of claim 11, 22, and 4-chloro-N-[(5-{[4-(butylamino)piperidin-1-yl]sulfonyl}thien-2-yl)methyl]benzamide of claim 40. Also, the appl. '074 does not enable for treating all disorder related to the inhibition of the JNK pathway. Applicants request that the rejection be withdrawn.

The claimed compounds of applications 10/088,090 and 10/381,197 are different from those claimed in this application. Applicants request that the rejection be withdrawn.

The claims of application 10/381,200 are directed to a generic sulfonyl hydrazide compound comprising the species claimed in this application. The compounds of the appl. '200 are useful for treating diseases of the autoimmune and neuronal system. The appl. '200 does not disclose that the sulfonyl hydrazide compounds are effective for treating Tyep II diabetes. The appl. '200 does not provide sufficient nexus between autoimmune and neuronal disorders and type II diabetes so that they are substantially related and can be treated with the same compounds. Also, the appl. '200 does not suggest selecting the specific compounds of

claim 11, 22, and 4-chloro-N-[(5-{[4-(butylamino)piperidin-1-yl]sulfonyl}thien-2-yl)methyl]benzamide of claim 40. Also, the appl. '200 does not enable for treating all disorder related to the inhibition of the JNK pathway. Applicants request that the rejection be withdrawn.

The claims of application 10/381,665 are directed to a generic sulfonyl hydrazide compound comprising the species claimed in this application. The compounds of the appl. '665 are useful for treating disorders modulated by abnormal expression of JNK, wherein the disorder is autoimmunity, ischemia or reperfusion. The appl. '665 does not disclose that the sulfonyl hydrazide compounds are effective for treating type II diabetes (one of many disorder modulated by the JNK pathway). The appl. '665 does not provide sufficient nexus between autoimmunity, ischemia or reperfusion and type II diabetes claimed in this application so that they are substantially related and can be treated with the same compounds. Also, the appl. '665 does not suggest selecting the specific compounds of claim 11, 22, and 4-chloro-N-[(5-{[4-(butylamino)piperidin-1-yl]sulfonyl}thien-2-yl)methyl]benzamide of claim 40. Also, the appl. '665 does not enable for treating all disorder related to the inhibition of the JNK pathway. Applicants request that the rejection be withdrawn.

The claims of application 10/484,744 are directed to a generic sulfonyl hydrazide compound comprising the species claimed in this application. The compounds of the appl. '744 are useful for treating apoptosis related disorder (e.g., cancer), inflammations, and cardiovascular disorders. The appl. '744 does not disclose that the sulfonyl hydrazide compounds are effective for treating type II diabetes. The appl. '744 does not provide sufficient nexus between, for example, apoptosis related disorders and inflammation, and tyep II diabetes so that they are substantially related and can be treated with the same compounds. Also, the appl. '744 does not suggest selecting the specific compounds of claim 11, 22, and 4-chloro-N-[(5-{[4-(butylamino)piperidin-1-yl]sulfonyl}thien-2-

yl)methyl]benzamide of claim 40. Also, the appl. '744 does not enable for treating all disorder related to the inhibition of the JNK pathway. Applicants request that the rejection be withdrawn.

The claims of application 10/070,954 are directed to a generic sulfonyl hydrazide compound comprising the species claimed in this application. The compounds of the appl. '954 are used for treating diseases associated with the abnormal expression or activity of JNK. The appl. '954 does not disclose that the sulfonyl hydrazide compounds are effective for treating of all JNK mediated disorders, and specifically, type II diabetes. Also, the appl. '954 does not suggest selecting the specific compounds of claim 11, 22, and 4-chloro-N-[(5-{[4-(butylamino)piperidin-1-yl]sulfonyl}thien-2-yl)methyl]benzamide of claim 40 for treating type II diabetes. Also, the appl. '744 does not enable for treating all disorder related to the inhibition of the JNK pathway. Applicants request that the rejection be withdrawn.

A Notice of Allowance for all pending claims is requested.

Respectfully submitted,

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